

Remarks

Claims 480-498 are presently pending in the subject application.

Reconsideration and allowance are respectfully requested in view of the above amendments and the following remarks.

Claims 422-429, 431-433, 440-448, 450-452, 459, 461-479 are canceled herein without prejudice to the prosecution of the subject matter of these claims in this or a future continuing application.

Claims 480-498 are newly added herein.

New claim 480, the only independent claim, corresponds to former claim 422 and further recites that the claimed probe is included in a kit comprising a nucleic acid polymerase, nucleotide triphosphates and an amplification oligonucleotide. The newly added subject matter of claim 480 is supported in the specification at, for example, page 28, line 20 *et seq.*, and page 33, line 3 *et seq.*

New claims 482, 484, 486 and 488-497 correspond to former claims 423-426, 466, 427-429, 422, 431-433 and 464, respectively.

New claims 481, 483, 485 and 487 depend from claims 480, 482, 484 and 486, respectively, and recite that the first base region complexes with the target nucleic acid sequence. This amendment is supported in the specification at, for example, page 21, lines 3-7.

New claim 498 depends from claims 480-497 in the alternative and recites that the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution. This claim language is supported in the specification *passim* and appeared in former claims 440 and 467-472.

Interview Summary

During a telephonic interview with the Examiner on January 5, 2006, the undersigned representative pointed out that the Examiner's Section 103 rejection based on Agrawal *et al.* (International Publication No. WO 94/01550) in view of Tyagi *et al.* (U.S. Patent No. 5,925,517) was analogous to a Section 103 rejection based on Lubini *et al.* (*Current Biology*, 1(1):39-45 (1994)) in

view of Tyagi *et al.* which issued in an Office Action mailed on April 4, 2005. The latter rejection was withdrawn in an Office Action mailed on August 12, 2005 based on remarks set forth in Applicants' Reply dated June 2, 2005. For this reason, the undersigned representative requested that the Examiner withdrawal the finality of the Office Action mailed on December 27, 2006. In a continuation of this telephonic interview on January 6, 2006, the Examiner agreed to withdraw the finality of the latest Office Action, indicating that a written response to this Office Action would be treated as a response to a non-final Office Action.

Rejection Under 35 U.S.C. § 103

Claims 422-429, 431-433, 440 and 466-472 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Agrawal *et al.* (International Publication No. WO 94/01550) in view of Tyagi *et al.* (U.S. Patent No. 5,925,517). As discussed below, Applicants respectfully submit that this rejection is rendered moot by the amendments to the claims herein.

Agrawal is cited for teaching a probe having first and second base regions that are capable of hybridizing to each other under nucleic acid assay conditions, with the resulting hybrid containing at least one 2'-O-alkyl substitution to a ribofuranosyl moiety. Agrawal is also cited for teaching that the probe forms a stable double-stranded complex with a nucleic acid analyte but not with a non-targeted nucleic acid under nucleic acid conditions, where the complex comprises a single-stranded form of the probe. Tyagi is cited for teaching oligonucleotides having self-complementary regions and a detectable label (*e.g.*, a fluorescent molecule). Thus, the Examiner contends that it would have been obvious to one of ordinary skill in the art at the time of the invention to have modified the oligonucleotide of Agrawal to include a label for the purpose of detecting the oligonucleotide hybridized to a target nucleic acid.

The claims newly presented herein are all directed to a probe, as recited in the previously pending claims, that is included in a kit which further comprises a nucleic acid

polymerase, nucleotide triphosphates and an amplification oligonucleotide. Agrawal does not suggest such a combination, as the oligonucleotides of Agrawal are only described as being useful as antisense oligonucleotides that resist nucleolytic degradation. *See, e.g.*, Agrawal at page 5, lines 2-12. Moreover, Tyagi does not suggest modifying the oligonucleotides of Agrawal for use in an amplification reaction, as Tyagi specifically teaches away from the use of self-hybridizing oligonucleotides requiring a strand displacement reaction for the oligonucleotide to hybridize to the target sequence, as would be required by the self-stabilized oligonucleotides taught by Agrawal. *See* Tyagi at col. 2, line 53, through col. 3, line 26; *see also* Agrawal at page 16, lines 24-35, and in Figures 1, 5 and 6. Tyagi also teaches probes having an affinity pair (*i.e.*, self-hybridized arm portions of the probe) that “reversibly interacts . . . sufficiently weakly that the hybridization of the target complement sequence and its target sequence is thermodynamically favored over the interaction of the affinity pair.” *See* Tyagi at col. 9, lines 45-50. Agrawal, on the other hand, teaches incorporating 2'-O-methyl ribonucleotides into the self-complementary region of a self-stabilized oligonucleotide to create a “hyperstabilized” oligonucleotide. *See* Agrawal at page 16, lines 24-29. Thus, the cited references fail to disclose or suggest the combination of the claimed invention.

The Examiner also contends that the inclusion of a conjugate molecule is taught by Agrawal (*see* new claims 490 and 491). In actuality, the section of Agrawal referenced by the Examiner teaches that an intercalating agent molecule may be used as an alternative to a 2'-O-methyl substitution in the self-complementary region or the target hybridizing region to render a self-stabilized oligonucleotide hyperstabilized. *See* Agrawal at paragraph bridging pages 16 and 17.

The Examiner further concludes that Agrawal teaches that the nucleic acid analyte may comprise ribosomal RNA (*see* new claim 496). In fact, that portion of Agrawal cited by the Examiner is limited to teaching that disease conditions may be treated by targeting a virus nucleic acid sequence. Since viruses do not contain ribosomal RNA, such cannot be taught by Agrawal.

AMENDMENT

Serial No. 09/808,558
Atty. Docket No. GP068-05.CN3

Additionally, the Examiner urges that Agrawal teaches that the target sequence may be contained within a double-stranded region (*see* new claim 497). To the contrary, in the section referenced by the Examiner, Agrawal merely discloses that the self-stabilized oligonucleotide, not the target nucleic acid sequence, contains a double-stranded region.

For the reasons set forth above, Applicants submit that the presently claimed invention is fully patentable in view of the cited references, considered alone or in combination.

Conclusion

In view of the above amendments and remarks, Applicants submit that the subject application is in condition for allowance and notice to that effect is respectfully requested.

Please charge the fees due in connection with this Amendment to Deposit Account No. 07-0835 in the name of Gen-Probe Incorporated.

Respectfully submitted,

Date: April 27, 2006

By: /Charles B. Cappellari/
Charles B. Cappellari
Registration No. 40,937
Attorney for Applicants

GEN-PROBE INCORPORATED
Patent Department
10210 Genetic Center Drive
San Diego, California 92121
PH: 858-410-8927
FAX: 858-410-8928